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Both the clinical and laboratory phases of this work are proceeding on schedule. We have reviewed the medical records of 782 individuals, confirming that 92 percent of them indeed had a mastectomy performed with prophylactic intent. The acquisition of complete risk factor information and important clinical follow-up data (specifically the occurrence of breast and non-breast cancer in these high-risk individuals) is underway via medical record review and patient/next of kin follow-up questionnaire. In this initial phase,prior to complete documentation with outside records, 14 potential cases of breast cancer following prophylactic mastectomy have been identified.

The laboratory investigators have developed appropriate screening methods for the ascertainment of BRCA1 mutations and several mutations have been identified. We have also developed techniques for the analysis of small breast lesions found in archival paraffin-embedded specimens, including atypia and lobular carcinoma in situ.

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Lynn C. Hartman
Principal Investigator's Signature

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Outcome After Prophylactic Mastectomy in Individuals at High Risk for Breast Cancer: A Combined Clinical Biological Study

Principal Investigator: Lynn C. Hartmann, M.D.

ANNUAL REPORT: INTRODUCTION

Breast Cancer: Options for Prevention - Medical

At the present time, options for breast cancer prevention are limited (1). Possible medical approaches include some manipulation of endocrine function, such as long-term use of tamoxifen or a contraceptive combination including a gonadotropin-releasing hormone agonist, low-dose estrogen and an intermittent progestogen (1). These approaches have major lifestyle implications, possible morbidities upon long-term application, and no proof of efficacy. The role of tamoxifen as a possible breast cancer preventive measure is currently the subject of a placebo-controlled trial. However, within the scientific community, there exists uncertainty regarding its possible net benefit (2,3). Moreover, recent additional data regarding tamoxifen's link with endometrial cancer have prompted recontacting all participants to inform them of its risks and the need for more aggressive follow-up for endometrial cancer (4). Early detection via an aggressive screening approach (or secondary prevention) is another option, utilizing the early initiation of mammography and regular breast self examinations and clinical breast examinations (5). However, no data exist to demonstrate the efficacy of this strategy in improving detection or reducing mortality for breast cancer (6). Moreover, the increased density of breasts of younger women may limit the sensitivity and specificity of mammography in this population (7,8). Some have quoted a false-negative rate with mammography in premenopausal woman as high as 40% (9). Thus, for individuals at substantial risk for breast cancer, no currently available medical approach to prevention is considered reliable and efficacious.

Breast Cancer: Options for Prevention - Surgical

Removal of the tissue at risk, namely prophylactic mastectomy (PM) represents an option for women at significantly increased risk of breast cancer. An extreme approach, prophylactic surgery currently is considered our most effective preventive maneuver, although its efficacy has not been systemically studied (see below).

At many centers, the most commonly performed PM is a subcutaneous mastectomy (SCM) (10). This procedure removes approximately 95% of breast glandular tissue but preserves the nipple-areolar complex, thus providing a more aesthetic result without the need for additional nipple reconstructive surgery (11-13). However, because some glandular breast tissue remains beneath the nipple, the procedure has been challenged as a prophylactic maneuver. In fact, in one rodent model of mammary carcinogenesis, prophylactic subcutaneous mastectomy failed to demonstrate a proportionate reduction in mammary cancer risk (14). In the medical literature, scattered reports exist of breast cancer developing in women after prophylactic subcutaneous mastectomy (15,16).

Because of concerns of incomplete protection with SCM, some practitioners recommend total mastectomy (TM), namely removal of the entire breast including the nipple-areolar complex, as the preferred prophylactic procedure (15). It should be noted, however, that controversy exists whether any mastectomy can be truly

prophylactic (17,18). In fact, even following total mastectomy or modified radical mastectomy, careful pathologic studies consistently identify residual breast tissue in the anterior chest wall or axillary tail (10,19).

Despite the utilization of PM for women at increased risk of breast cancer, we have incomplete data regarding its efficacy. Long-term rigorous, systemic follow-up of a large and uniformly treated population has not been done (17). Data regarding qualify of life, complications, the need for repeat breast surgeries, and the occurrence of breast and non-breast cancers in these women are also lacking (9). Moreover, there has been inadequate definition of the underlying risk of the various populations undergoing this procedure.

Genetic Susceptibilty Testing: An Immediate Challenge

The identification within the past year of the first major human susceptibility gene for breast cancer, BRCA1, (20), the localization of additional breast cancer susceptibility genes, e.g. BRCA2 (21) along with the rapid development and marketing of commercially available genetic testing raises several concerns (22). At present, the medical community's diagnostic capabilities exceed our prevention offerings for high-risk women. For such time as prophylactic mastectomy is considered the most efficacious approach for these individuals, we must be able to provide patients and providers with appropriate follow-up information regarding the procedure's efficacy and side effects. As was recently stated by the American Society of Human Genetics:

> Women in high-risk families should be informed about the risks, benefits, and limitations of predictive testing and about the uncertainty about the effectiveness of current monitoring and prophylactic interventions . . . . As yet, no proved methods of primary prevention for breast or ovarian cancer exist. Prophylactic mastectomy or oophorectomy may be effective, but the results of systematic long-term follow-up to determine the frequency of cancer in residual tissue or in other organs are not available. Research to evaluate the efficacy and risks of monitoring and prevention strategies is essential to determine if genetic testing translates into reduction of morbidity and mortality for breast and ovarian cancer and to determine if specific management approaches have adverse outcomes (23)

This point was also emphasized in a recent JAMA review:

> Advances in molecular genetics have provided data that allow risk estimation for women with inherited mutations in dominant cancer susceptibility genes. Unfortunately, studies that allow estimation of risk reduction from prophylactic surgical intervention are essentially unavailable, and the science of chemoprevention is in its infancy. Furthermore, there are limited data available to assess the efficacy of enhanced surveillance programs for individuals at high risk for developing breast cancer (24).

Purpose of Present Work

The purpose of the present work is to determine the clinical outcome of a large population of women who had prophylactic mastectomy at the Mayo Clinic for increased risk of breast cancer; we will also determine outcome in BRCA1 carriers.

General Methods of Approach

We recognize the heterogeneity of our large patient population electing prophylactic mastectomy over a period of almost 25 years (1966 thru 1987). Our general approach to the problem is twofold: First, we will determine the expected risk of the individuals undergoing this procedure and second, we will determine their actual outcome. To determine the expected risk, a baseline breast cancer risk assessment, based on factors pertinent at the time of prophylactic mastectomy, will be calculated for each patient. This risk will be based on family history information, history of benign breast disease, and reproductive factors (see Appendix I). Given the identification of BRCA1 within the last year, we will also identify BRCA1 carriers from those individuals with appropriate family histories. The expected likelihood of breast cancer in BRCA1 carriers has been reported to approach 85 percent over a woman's lifetime (25,26).

To determine the actual outcome of these individuals, we are utilizing a thorough review of the medical record, as well as a detailed follow-up patient questionnaire that will be mailed to all living individuals and a similar questionnaire mailed to next of kin if the prophylactic mastectomy patient is known to be deceased. The outcome information will include cancer occurrences - breast, ovary, colon, or other; post-prophylactic mastectomy surgical morbidities and various measures of psychosocial satisfaction (seeking sources of funding for the latter studies) (Appendix I).

ANNUAL REPORT: BODY

Experimental Methods - Clinical

Chart Review: To date, we have reviewed the charts on 782 individuals listed in the Mayo Data Base as having had prophylactic mastectomy. Of these, 61 have been excluded from further participation because of the following reasons: Having had prior history of breast cancer - 15; breast cancer suspected and confirmed at time of surgery - 44; cosmetic surgery only - 2. Thus, out of this initial group of 782 patients listed in our surgical records as having had prophylactic mastectomy, a total of 721 (92.2%) have been found at official chart review to, in fact, have had a prophylactic mastectomy. During this chart review, information about vital status, breast surgeries, breast cancer subsequent to prophylactic mastectomy, other cancers, and various risk factors for breast cancer have been abstracted from the patient record (see Appendix II).

Follow-up Questionnaire: Appropriate follow-up questionnaires were developed for each possible category of patient electing prophylactic mastectomy (see

Appendix III). Following completion of chart review, the appropriate set of follow-up questionnaires is sent to the patient or next of kin (if patient deceased). Thus far, a total of 408 questionnaires have been sent; the first mailings were sent on June 27, 1995. Thus far, 203 individuals have returned completed forms. Seven individuals indicated that they did not want to participate. The other forms are outstanding as of July 31, 1995. Second mailings will be sent to follow the unanswered questionnaires. Telephone follow-up will be utilized as needed.

Clinical Outcomes: Breast Cancer: As of 7-31-95, based on the nurse abstractor's review of the patient charts, a total of 14 possible cases of breast cancer following prophylactic mastectomy have been identified. These are preliminary data as we await necessary documentation and physician review of these cases.

Experimental Methods - Laboratory

Histopathologic Review: We have developed a system for the acquisition of tissue blocks and slides for all cases confirmed by chart review to represent prophylactic mastectomy. These will be reviewed and characterized by Dr. T. Crotty, Surgical Pathology.

BRCA1 Mutation Detection: During the first year of the project, we have been developing methods for the detection of mutations in the BRCA 1 gene in our prophylactic mastectomy cohort. Such methods will need to ascertain accurately the BRCA1 carriers in this cohort, so as to assess the preventive capability of prophylactic mastectomy in this highest risk group. Our strategy is to develop technically simple, sensitive, and specific screening assays for as many of the currently known BRCA1 mutations (20,27-32) as possible.

Our first screening method involves the use of restriction endonucleases. Some known BRCA 1 mutations either create a new restriction enzyme site or remove an existing site; both situations can be distinguished easily from wildtype DNA on appropriate agarose gels. In some situations the mutation does not create or delete a site; we then induce an artificial site by the use of a PCR primer with a predesigned mismatch (AIRS=Artificial Induction of Restriction Sites) (33-40). A second screening method is to PCR amplify an exon of interest and then to electrophorese the resulting product on a gel of high agarose content. An insertion or a deletion of greater than three base pairs is unambiguously detected by this assay.

Many known (and most unknown) BRCA 1 mutations, cannot be detected by these initial screening methods. To ascertain additional mutations, we are using single stranded conformational polymorphism (SSCP) analysis (31). Although this assay will only detect mutations that alter the secondary structure of individual DNA strands, it has the advantage of detecting new, unpublished mutations. The final mutation screening assay we are using is the Protein Truncation Test (PTT) (41-43). It involves amplifying genomic DNA with a modified PCR primer and then evaluating that product in a coupled transcription/translation reaction. Nonsense or frameshift mutations which result in a truncated protein are detected as novel discrete bands on a SDS-polyacrylamide gel. This assay is useful for screening

exon 11 of the BRCA1 gene, which encodes 61 percent of the gene. Nonsense and frameshift mutations are common in this exon (27-32). Table 1 compiles the published (20, 27-31) and unpublished (32) BRCA1 mutations to date and lists the assays we will use to screen for these mutations.

Our strategy is to apply these screening assays to all patients in our prophylactic mastectomy cohort with a family history of breast cancer. To determine the specificity of our screening methods, we will evaluate all potentially positive specimens by DNA-sequencing. To evaluate the sensitivity of our screening methods, we will also evaluate multiple negative specimens by DNA-sequencing. In the course of these studies we may find that it may be necessary to DNA-sequence some exons from the start if our screening methods are not very accurate.

We have isolated DNA from 10 patients who have a positive breast/ovarian cancer family history and have begun to evaluate them using the above BRCA mutation screening and DNA-sequencing strategy.

Using SSCP, agarose gel, and AIRS, we detected a germline exon 16 mutation in one patient. DNA-sequencing revealed a mutation similar to the published 5085 del 19 → ter 1671 mutation; our patient's mutation was 5083 del 19 → ter 1671. This mutation clearly disrupts the reading frame of the BRCA1 mRNA and very likely results in a nonfunctional protein. In addition, we have also found a second germline exon 15 mutation (4719 Glucose -> A, Val 1534Met) in this patient. This missense mutation may very well be a normal DNA polymorphism and we are evaluating a control population to test this hypothesis. In a second patient, we also observed an unpublished exon 5 mutation. This mutation, 310 G→ A, Cys64Tyr, removes the last cysteine of the zinc finger DNA-binding motif of BRCA1. Other mutations in this cysteine and in other cysteines of this motif have been previously reported to be linked with breast cancer in some BRCA families (31). Thus, it is very likely that the germline mutation we observed is causative in this patient. All of the above mutations were verified by sequencing the DNA in both directions. Through SSCP we recently discovered what could be either a DNA-polymorphism or a novel mutation in exon 9 in 4 of these 10 patients. We are currently DNA-sequencing these 4 specimens to define the underying sequence alteration. We are also testing a control population to determine if the alteration is a polymorphism or a new mutation.

<u>Analysis of Concomitant Benign Breast Tissue and Lobular Carcinoma in Situ (LCIS):</u>
One of the strengths of this work is the opportunity to examine matching benign breast tissue from the contralateral breast (removed prophylactically) in women who have breast cancer specimens at Mayo (removed via radical/modified radical mastectomy). In addition, LCIS specimens can be compared with benign specimens from the same patient. These analyses require the development of inexpensive and practical techniques for isolating DNA from small paraffin-embedded breast lesions. To this end, we developed an inexpensive and reproducible DNA isolation technique using paraffin-embedded tissue sections mounted on cellulose acetate sheets. Regions of interest can be removed from the sheet using a scalpel. This simple technique greatly improved the yield of selected

cell populations (> 84 percent), thereby decreasing contamination by surrounding normal tissue DNA. This is a significant contribution since ≥ 20 percent normal cells can mask loss of heterozygosity (LOH). For example, Figure 1 exemplifies the small areas of atypical cells used for DNA amplification.

DNA isolated from paraffin-embedded tissue is often fragmented and very small, therefore all PCR parameters, especially template denaturation, primer annealing and extension times were optimized. In our experience, only 20 percent of microsatellite markers are efficacious on paraffin DNA. Extensive testing of primer pairs was required for optimal DNA alleotype resolution. See Figure 2 for examples of PCR allele patterns. Compared with previously published reports using paraffin-DNA, our banding results are excellent. Improved band resolution allows more accurate LOH determination.

Initially, 16 breast cancer specimens were evaluated by this new technique. Normal breast DNA was isolated from corresponding contralateral prophylactic mastectomy tissue. As depicted in Figure 3, the regions and frequency of LOH on chromosome 17 were comparable to previously reported data using fresh frozen breast cancer DNA. However, there was an unacceptably high indeterminate rate secondary to the small amounts of normal control ductal tissue available in breast specimens from observation from older women. Subsequently, normal control lymph node DNA and breast cancer DNA from each patient yielded a significant decrease in indeterminate DNA patterns. To ensure that breast cancer cells were not present in the lymph node tissue utilized for DNA isolation, immunohistochemical techniques with anticytokeratin antibodies were employed.

We next used these optimized conditions to isolate very small areas of premalignant/malignant changes in human breast tissue. The new microdissection technique could isolate approximately 20 to 100 cells. The DNA isolated from such a small number of cells was successfully amplified by our PCR conditions. Recently, we evaluated 18 specimens of atypical ductal hyperplasia, LCIS and ductal carcinoma in situ (DCIS) for LOH in the regions of BRCA1 and BRCA2. Our results showed 15 percent LOH for the BRCA2 region in LCIS specimens and approximately 10 percent LOH for the BRCA1region in DCIS specimens. Figure 4 illustrates an example of LOH for these small lesions. Of interest, the areas of genetic loss are extremely small, emphasizing the need for optimal techniques for evaluation of early breast lesions.

CONCLUSIONS:

The primary question posed in this work, namely the efficacy of prophylactic mastectomy in women at high risk for breast cancer, is even more timely today than when this grant was first submitted. The identification of breast cancer susceptibility genes and the rapid development of commercially available testing for carriers of mutations in these genes will soon permit more precise risk assessment from many women from breast cancer families. Until alternative preventive measures for breast cancer are available, it is imperative that the medical community have complete follow-up information regarding prophylactic mastectomy to be able to present this option realistically to individual women. To

inform a woman that she is a carrier of a breast cancer predisposing gene, and thus at very high risk for breast cancer, and to tell her that prophylactic mastectomy is an option but that we lack follow-up data regarding its efficacy or side effects, is unacceptable. Besides studying the clinical outcomes of women who have had prophylactic mastectomy (i.e. cancer occurrences and post-surgical morbidities), we are also asking women to comment on various psychosocial measures following prophylactic mastectomy. This information is being collected, and we are attempting to find funding for the appropriate analyses of these psychosocial data.

During this first year of the grant award, we have demonstrated the following:

1. Accuracy of the Mayo Clinic's surgical listing of prophylactic mastectomy. Of the 782 charts abstracted thus far, 92.2 percent have indeed been confirmed to have had prophylactic mastectomy.

2. Feasibility of combined chart review and patient/next of kin questionnaire to obtain complete risk factor information and clinical follow-up data

3. Establishment of satisfactory mechanisms for obtaining and review of histopathologic material

4. Ability to detect BRCA1 germ line mutations in very high risk individuals

5) Ability to isolate DNA from small paraffin-embedded specimens of benign breast lesions, and LCIS for comparative genetic analyses.

Thus, we are on schedule to complete the scope of the work described in our grant, DAMD 17-94-J-4216.

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Table: Mutation Screening Assays for Known BRCA1 Mutations

Exon	Codon Mutation	Base Mutation & Terminal Codon if Applicable	Mutation Screening Available
Ex. 2	23 del AG	185 del AG-> ter39	SSCP, AIRS
Ex. 2	24 del 11	188 del 11-> ter 39	SSCP,Agarose
Ex. 5	Cys 61 Gly	300 T -> G	SSCP, NRS
Ex. 5	Cys 64 Gly	309 T-> G	SSCP
In. 5		T->G->ins59->ter75	Agarose
In. 5		331 + 2T-> C	NA
Ex. 8	Gln 169 ter	624 C-> T	SSCP, AIRS??
Ex. 11	266 del TT	916 del TT-> ter 285	PTT
Ex. 11	270 ins 11	926 ins 11-> ter 301	PTT, Agarose
Ex. 11	339 ins A	1128 ins A-> ter 345	PTT
Ex. 11	361 del 11	1201 del 11-> ter 361	PTT, Agarose, NRS??
Ex. 11	392 del 40	1294 del 40-> ter 398	PTT, Agarose
Ex. 11	407 ins C	1339 ins C	PTT
Ex. 11	Gln 526 ter	1695 C-> T	PTT
Ex. 11	Gln 562 ter	1806 C-> T	PTT
Ex. 11	Leu 639 ter	2035 T-> A	PTT
Ex. 11	654 del A	2073 del A	PTT
Ex. 11	655 ins A	2080 ins A-> ter 672	PTT
Ex. 11	720 ins A	2278 ins A	PTT
Ex. 11	725 del G	2294 del G-> ter 735	PTT, NRS??
Ex. 11	766 del AG	2415 del AG-> ter 766	PTT
Ex. 11	Thr826Lys	2596 C-> A	??
Ex. 11	826 del C	2477 del C-> ter 845	PTT
Ex. 11	894 del A	2800 del A-> ter 901	PTT
Ex. 11	Glu 908 ter	2841 G-> C	PTT
Ex. 11	915 del TC	2863 del TC-> ter 915	PTT, NRS??
Ex. 11	956 del 5	2982 del 5-> ter 968	PTT, NRS??
Ex. 11	1002 del A	3121 del A-> ter1023	PTT
Ex. 11	1016 ins 5	3166 ins 5-> ter 1025	PTT
Ex. 11	1160 del 11	3598 del 11-> ter 1166	PTT, Agarose, NRS??
Ex. 11	Leu 1081 ter	3358 T-> A	PTT
Ex. 11	1111 del 4	3450 del 4-> ?ter 1085	PTT
Ex. 11	Arg 1203 ter	3726 C -> T	PTT, NRS??
Ex. 11	1234 del A	3821 del A-> ter 1242?	PTT, NRS??
Ex. 11	Glu 1250 ter	3867 G -> T	PTT, NRS??
Ex. 11	1252 del 4	3875 del 4-> ter 1262	PTT
Ex. 11	1259 del T	3896 del T-> ter1263	PTT
Ex. 11	1290 del AA	3986 del AA-> ter 1293	PTT
Ex. 11	Gln 1313 ter	4056 C->T	PTT, NRS??
Ex. 11	1355 del 4	4184 del 4-> ter 1364	PTT
Ex. 11	Gln 1395 Gln	4304 G-> A	??
Ex. 13	Arg 1443 Gly	4446 C -> G	SSCP
Ex. 13	Arg 1443 ter	4446 C -> T	SSCP
In. 13		4476 + 6T-> C	Agarose??
Ex. 15	Glu 1541 ter	4740 G->T	SSCP, NRS
Ex. 16	Tyr 1563 ter	4808 C-> G	SSCP, AIRS??
Ex. 16	Pro 1637 Leu	5029 C->T	SSCP, NRS
Ex. 16	1656 del 19	5085 del 19-> ter 1671	SSCP, Agarose
Ex. 18	Ala 1708 Glu	5242 C->A	SSCP, AIRS
In. 18		del A->del exon 19->ter 1732	??
In. 18		5271 + 1G-> T	??
Ex. 19	Lys 1727 ter	5298 A-> T	SSCP
In. 19		5312 + 2 del T	??
Ex. 20	1756 ins C	5382 ins C-> ter 1829	SSCP
Ex. 21	1773 ins C	5438 ins C-> ter1829	SSCP
Ex. 21	Met 1775 Arg	5443 T->G	SSCP, AIRS
Ex. 24	Arg 1835 ter	5622 C-> T	SSCP, AIRS??
Ex. 24	1837 del G	5629 del G	SSCP
Ex. 24	1853 ins A	5677 ins A-> ter 1853	SSCP, AIRS

Agarose = PCR amplification followed by agarose gel electrophorese
AIRS = Artificial Induction of Restriction Site
NRS = Natural Restriction Site
PTT = Protein Truncation Test
SSCP = Single Stranded Conformation Polymorphism
?? = Test still being developed

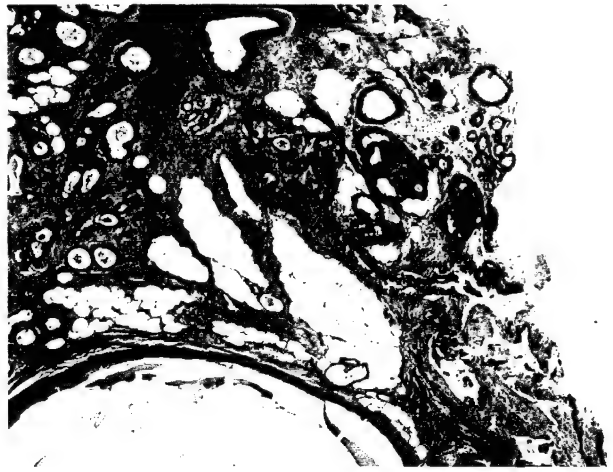

Figure 1: Circled area illustrates a region of atypia used for DNA amplification.

Marker: D17S807

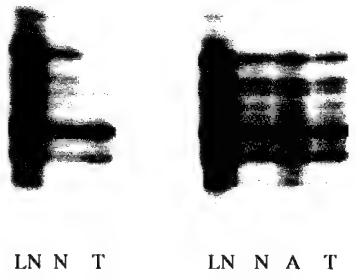

Figure 2: Microsatellite evaluation of LOH in the BRCA1 region. Specimens from two women with breast cancer are illustrated. LN=lymph node DNA; N=normal breast duct DNA; A=atypical duct DNA; T=breast cancer DNA. Concentrations of each DNA sample were adjusted to give comparable band intensity for LOH determination. Figure on left represents LOH in tumor tissue with loss of upper band intensity.

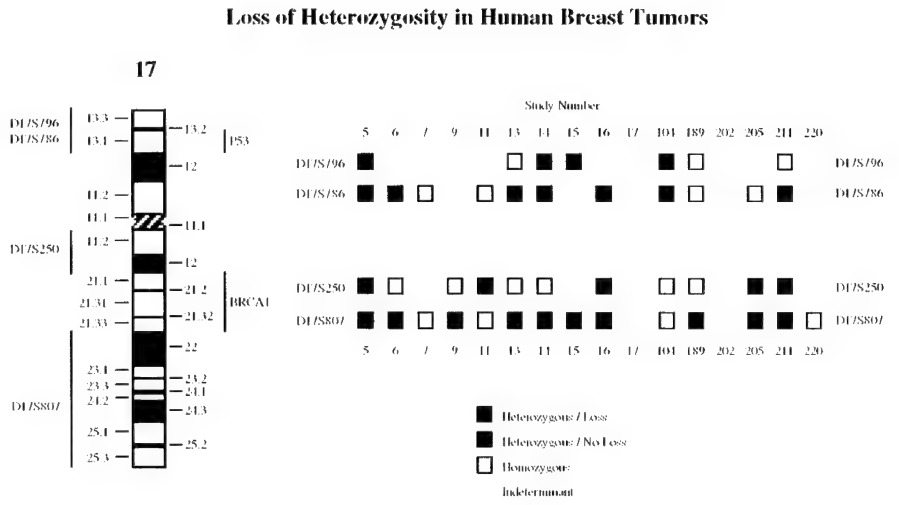

Figure 3: An Allelotype of chromosome 17 showing frequency and location of genetic losses in paraffin-embedded breast cancer DNA.

Marker: D13S290

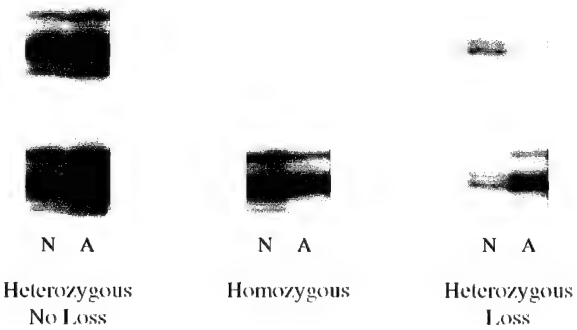

Figure 4: Microsatellite evaluation of LOH in the BRCA2 region. Specimens from three women with atypia are illustrated. Normal breast duct DNA; a=atypical (carcinoma in situ) ductal DNA. Notice loss of bands in atypia lane representing LOH.

Mayo Clinic

200 First Street Southwest Rochester, Minnesota 55905 Telephone 507 284-2511

You had a prophylactic mastectomy (preventive removal of the breast) performed by Mayo Clinic's plastic surgeons. Dr. John E. Woods and Dr. P. G. Arnold from the Department of Surgery at Mayo and I would like to ask you for some information.

Our primary purpose in contacting you at this time is to assess your particular reasons for having had a prophylactic mastectomy and to ask how your health has been following that surgery. In this packet, you will find a form containing questions about your family history of breast cancer, as well as your menstrual and reproductive history. We will also ask about any breast problems that you may have had since your prophylactic mastectomy, including the possibility of any breast cancer or the need for any additional breast surgery. We will also ask you whether you have developed any other cancers.

This follow-up work that we are now doing is part of an approved Mayo Clinic study. We hope that the follow-up information learned through this study will help physicians counsel women in the future as they think about having a prophylactic mastectomy performed. As with your other Mayo Clinic records, the information that you provide us will be kept strictly confidential.

We would like to emphasize that the reason for asking these questions is not that we are concerned about silicone implants causing cancer. Most women who had prophylactic mastectomy at Mayo did so because of a concern about breast cancer. These concerns were based on a variety of reasons, including pre-cancerous change in the breast, a history of breast cancer in the family, or having had multiple prior biopsies for suspicious lumps in the past. These factors are known to increase a woman's risk of a breast cancer to some extent. Some of these factors have also been associated with the development of other types of cancer, such as ovarian cancer or colon cancer. Thus, it is important that we learn of any breast or non-breast cancer problem that you may have had.

We would like to address the concerns that have been raised in the press about silicone implants and their possible health hazards, including links with breast cancer and several arthritis-like conditions (also called connective tissue diseases). We would like to update you regarding the status of well-controlled medical studies of patients who have had silicone implants. A recently completed Mayo Clinic study looked at the

development of arthritis-like illnesses in Rochester-area women who had silicone-containing implants. Mayo investigators saw no evidence for a link between these implants and any connective tissue disease. These results have been published recently in The New England Journal of Medicine. Moreover, a Canadian group recently studied women who had breast augmentation (or enlargement), with implant placement, for any evidence of later increased breast cancer risk. In fact, these investigators saw fewer breast cancers in women who had implants compared with women in the general population (N Engl J Med, Berkel et al, June 18, 1992). This finding by no means indicates that implants lower risk, but we have no reason to think that they contribute to breast cancer.

We appreciate your help in this study and hope that you are willing to provide the information. If you do not wish to complete the questionnaire, please indicate this below and return this letter since it will make a follow-up call unnecessary. Please understand that current or future medical care at the Mayo Clinic for you and your family members will not be affected by your decision. Specifically, your care will not be jeopardized if you choose not to complete the questionnaire.

If you have family members with breast cancer, and indicate so on the enclosed form, we will be contacting you again for more detailed family information.

We thank you for your consideration.

Sincerely yours,

Lynn C. Hartmann, M.D.
Mayo Women's Cancer Program

John E. Woods, M.D.
Department of Surgery

Phillip G. Arnold, M.D.
Department of Surgery

☐ I do not wish to participate further in this survey.

KPOO

PROPHYLACTIC MASTECTOMY FOLLOW-UP STUDY

SURVEY RESEARCH CENTER

mayo

1-7

Please enter above any missing information or change any that is incorrect.

Instructions: Please check the appropriate box or fill in the blank as indicated.

8-13 **Today's Date** _____/_____/_____
Month Day Year

MEDICAL HISTORY

WE ARE INTERESTED IN THE MEDICAL HISTORY AND FAMILY HISTORY OF WOMEN WHO HAVE CHOSEN TO HAVE A PROPHYLACTIC MASTECTOMY.

14-15 **1. At what age did you begin menstruating?**

__ __ _____ years

16__ **2. Have you had children?**

1 ☐ No 2 ☐ Yes

17-18 **How old were you when your first child was born?**
__ __ _____ years

19__ **3. Did you have any breast biopsies before your prophylactic mastectomy?**

1 ☐ No 2 ☐ Yes

20-21 **How many breast biopsies did you have before your prophylactic mastectomy?**
__ __ _____ Number of breast biopsies

22__ **Did any of the biopsy results show worrisome findings?**
1 ☐ No 2 ☐ Yes

23__ **4. Has your (blood-related) mother had breast cancer?**

1 ☐ No 2 ☐ Yes 3 ☐ Don't know

24-27 **If yes, in what year?** _____

28-31 **What is her year of birth?** _____

32__ **5. Do you have any blood-related sisters?**

1 ☐ No 2 ☐ Yes

33-34 **If yes, how many?** _____

__ __

35__ **Have any of your sisters had breast cancer?**
(Do not include yourself in responding to this question.)

1 ☐ No 2 ☐ Yes

SISTER #1

36-39 **If yes, in what year?** _____

40-43 **What is her year of birth?** _____

SISTER #2

44-47 **In what year?** _____

48-51 **What is her year of birth?** _____

SISTER #3

52-55 **In what year?** _____

56-59 **What is her year of birth?** _____

SISTER #4

60-63 **In what year?** _____

64-67 **What is her year of birth?** _____

SISTER #5

68-71 **In what year?** _____

72-75 **What is her year of birth?** _____

76__ **6. Do you have any blood-related daughters?**

1 ☐ No 2 ☐ Yes

77-78 **If yes, how many?** _____

79__ **Have any of your daughters had breast cancer?**

1 ☐ No 2 ☐ Yes

DAUGHTER #1

80-83 **If yes, in what year?** _____

84-87 **What is her year of birth?** _____

DAUGHTER #2

88-91 **In what year?** _____

92-95 **What is her year of birth?** _____

DAUGHTER #3

96-99 **In what year?** _____

100-103 **What is her year of birth?** _____

DAUGHTER #4

104-107 **In what year?** _____

108-111 **What is her year of birth?** _____

DAUGHTER #5

112-115 **In what year?** _____

116-119 **What is her year of birth?** _____

120__ **7. Have other blood relatives of yours, including men in the family, had breast cancer?**

1 ☐ No 2 ☐ Yes

121__ **If yes, please list relative .** _____

_____

_____

_____

122__ **8. Have any of your blood relatives had ovarian cancer?**

1 ☐ No 2 ☐ Yes

CANCER PROBLEMS

123__ **9. Have <u>you</u> ever been diagnosed with breast cancer?**

1 ☐ No 2 ☐ Yes

124-127 **If yes, in what year?** _____ year

128__ **In which breast?** 1 ☐ Right 2 ☐ Left

129-130 **What treatment did you have?** _____

_____

_____

131__ **Did your breast cancer ever spread?**

1 ☐ No 2 ☐ Yes

132-133 **If yes, where?**

_____

134-137 **In what year was this discovered?**

_____ year

138-139 **What treatment did you have?**

_____

_____

_____

10. Have you had any other cancers?

		<u>No</u>	<u>Yes</u>	<u>What year was cancer found?</u>
140-144	**Ovarian cancer**	1 ☐	2 ☐	_____
145-149	**Colon cancer**	1 ☐	2 ☐	_____
150-154	**Uterine cancer**	1 ☐	2 ☐	_____

Other cancer(s) (please list)

155-160	_____	_____
161-166	_____	_____
167-172	_____	_____
173-178	_____	_____

253__ **17. Overall, how satisfied are you with your prophylactic mastectomy(ies)?**

1 ☐ Very satisfied 2 ☐ Satisfied 3 ☐ Neither 4 ☐ Dissatisfied 5 ☐ Very dissatisfied

254__ **Please explain your reasons for your answer to this question.**

_____

_____

_____

_____

_____

255__ **18. Knowing what you do now, would you choose to have prophylactic mastectomy(ies) if you had it to do over again?**

1 ☐ Definitely would 2 ☐ Probably would 3 ☐ Unsure 4 ☐ Probably would not 5 ☐ Definitely would not

256__ **Please explain your reasons for your answer to this question.**

_____

_____

_____

_____

_____

257__ **19. Knowing what you do now, would you choose to have breast reconstruction after prophylactic mastectomy(ies) if you had it to do again?**

1 ☐ Definitely would 2 ☐ Probably would 3 ☐ Unsure 4 ☐ Probably would not 5 ☐ Definitely would not

258__ **Please explain your reasons for your answer to this question.**

_____

_____

_____

_____

_____

FSEDIT Modify

PROPHYLACTIC MASTECTOMY: Study 15942

_____ Mayo

_____ SSN

Name _____ _____ - _____ _____

Address _____

_____

_____

City _____ State __ Zip Code _____ Plus Four ____

Country _____

Telephone _____ Spouse _____

Other names _____

_ Sex

__ Race C=Caucasian B=Black AI=Am.Indian AN=Alaska Native AS=Asian
H=Hispanic PI=Pacific Islander O=Other,spec _____ U=Unknown

_ Status A=Alive D=Dead _ Death Indicator Y=Dead N=Alive

_____ Date of Birth ___ Age at PM _____ Date of Death

_____ Date of last follow-up _____ Last registration

_ EXCLUDE (0-4, ?=code window)

_ s1594201 Mayo breast surgery

_ s1594202 Family hx cancer _____ Date abstracted

_ s1594203 Tissue tracking ___ Abstractor JLJ,RSM

FSVIEW: IN.S1594201 (E) (Subset)

CLINIC	DTESURG	TYPE	S	PM	C1	C2	C3	R1	R2	R3	R4

FSEDIT Modify

_____ Mayo _____ Right Index _____ Left Index

BREAST CANCER PRIOR TO PROPHYLACTIC MASTECTOMY DIAGNOSED ELSEWHERE

_ Breast Cancer prior to PM diagnosed outside of Mayo (y=yes n=no)

_____ Date of breast ca dx EW _ Side of breast cancer (r/l)

_ Path reports available (y=yes n=no) _____ Date read at Mayo

_ _ _ Cancer pathology from EW/lab sheets (use cancer codes s1594201)

BREAST CANCER SUBSEQUENT TO PM on PM Side (Mayo or other inst.)

_ Breast cancer following PM (y=yes n=no)

__ Institution* _____ Date of breast cancer _ Side _ Site*

_ Path rep't available (y=yes n=no) _____ Date read at Mayo

_ _ _ Cancer pathology from EW/lab sheets (use cancer codes S1594201)

__ Institution* _____ Date of breast cancer _ Side _ Site**

_ Path rep't available (y-yes n=no) _____ Date read at Mayo

_ _ _ Cancer pathology from EW/lab sheets (use cancer codes s1594201)

*Institution: (M=Mayo S=Scottsdate J=Jacksonville EW=Elsewhere)

**Site: 1=Residual breast tissue 2=Chest wall 3=Axillary node
4=Supraclavicular node 5=????

FSEDIT Modify

_____ Mayo _____ Right Index _____ Left Index

OTHER PRIMARY CANCERS

_ Other Primary cancers (y=yes n=no)

_ 1=Ovarian 2=Colon 3=Uterine 0=Other,specify _____

_____ Date of other cancer

_ Second other primary cancer (code above)

0=Other,specify _____

_____ Date of other cancer

BENIGN BREAST BIOPSIES ELSEWHERE

__ Total number of BBB elsewhere prior to Prophylactic Mastectomy
(enter 99 multiple biopsies, but number unknown)

MAMMOGRAMS

_ Mammogram before PM at Mayo (y/n) _____ Date closest to PM

__ Number of mammograms at Mayo (10 year window prior to PM)

_ Mammogram from elsewhere, read at Mayo _____ Date read at Mayo

GENETIC REVIEW

_ Genetics Review (y/n) _____ Date of Genetics Review

FSEDIT Modify

_____ Mayo _____ Right Index _____ Left Index

RISK FACTORS AT TIME OF PM (enter one field only) (.u if unknown)

__ Age at menarche ____ Year of menarche

__ Age at birth of first child _____ Date of birth of first child

__ Menopause 1=Pre-menopause 2=Post-menopause (.u=unknown)

__ Age at Menopause _____ Date of menopause (.u=unknown)

__ IF Post-Menopausal 1=Natural 2=Artificial
3=Hormone Replacement Therapy .u=unknown

_ Cessation of menses 1=Hyst, no ooph 2= Hyst, unilat ooph 3=TAH/BSO
4=Bilat. ooph 5=Hyst. no info on ooph
6=Post chemo 7=Post radiation

___ Height in cm ___ Height in inches

___ Weight in kg ___ Weight in pounds

__ Gravidity __ Parity (any live birth)

_ Questions/Review MD _ Questions for RN

Comments _____

FSEDIT Modify

_____ Mayo

DEATH CERTIFICATE INFORMATION

_ Death Certificate available* (Y=yes N=no R=requested)

_____ Date requested

* Death Certificate not available from:
Alabama, Idaho, Indiana, New Jersey,
New York, North Dakota, and Onterio,
Canada

_ Breast cancer noted on Death Certificate (Y=yes N=no)

__ if yes, 1=Immediate cause 2=Consequence of .u=Unknown

_ Other cancers noted on Death Certificate

__ if yes, 1=Ovarian 2=Colon 3=Uterine .o=other,specify _____

FSEDIT Modify

_____ Mayo
Follow-up Screens

_____ Date to Follow-up (Survey Research Center)

_ No Contact (X = no contact)

_____ Date Follow Up Complete

Comments _____

Bilateral:patient deceased
Appendix III

Mayo Clinic

200 First Street Southwest Rochester, Minnesota 55905 Telephone 507 284-2511

Date

REGARDING: Ms. 8~

Our records indicate that you are the next of kin of Ms. 8~, who had a prophylactic mastectomy (preventive removal of the breast) performed by Mayo Clinic's plastic surgeons. We understand that Ms. 9~ is deceased. Dr. John E. Woods and Dr. P. G. Arnold from the Department of Surgery at Mayo and I would like to extend our sympathy to you and would also like to ask you for some information.

Our primary purpose in contacting you at this time is to clarify Ms. 9~'s reasons for having had a prophylactic mastectomy and to ask a few health-related questions pertaining to her life after her prophylactic mastectomy. In this packet, you will find a form containing questions about her family history of breast cancer and her menstrual and reproductive history. We will also ask about any breast problems that she may have had following her prophylactic mastectomy, including the possibility of any breast cancer or the need for additional breast surgery. We will also ask whether she developed any other cancers.

This follow-up work that we are now doing is part of an approved Mayo Clinic study. We hope that the follow-up information learned through this study will help physicians counsel women in the future as they think about having a prophylactic mastectomy performed. As with Ms. 9~'s other Mayo Clinic records, the information that you provide us will be kept strictly confidential.

If Ms. 9~ had family members with breast cancer and you indicate so on the enclosed form, we may contact you again about the possibility of obtaining more detailed family information.

We appreciate your help in this study and hope that you are willing to provide the information. If you do not wish to complete the questionnaire, please indicate this below and return this letter since it will make a follow-up call unnecessary. Please understand that current or future medical care at the Mayo Clinic for you and your family members will not be affected by your decision. Specifically, your care will not be jeopardized if you choose not to complete the questionnaire.

We thank you for your consideration.

Sincerely yours,

Lynn C. Hartmann, M.D.
Mayo Women's Cancer Program

John E. Woods, M.D.
Department of Surgery

Phillip G. Arnold, ~~M.D.~~
Department of Surgery

☐ I do not wish to participate further in this survey.

KPOO

PROPHYLACTIC MASTECTOMY FOLLOW-UP STUDY

SURVEY RESEARCH CENTER

1-7

Please enter above any missing information or change any that is incorrect.

Instructions: Please check the appropriate box or fill in the blank as indicated.

8-13 **Today's Date** _____/_____/_____
Month Day Year

MEDICAL HISTORY

WE ARE INTERESTED IN THE MEDICAL HISTORY AND FAMILY HISTORY OF WOMEN WHO HAVE CHOSEN TO HAVE A PROPHYLACTIC MASTECTOMY. PLEASE PROVIDE US WITH THE FOLLOWING INFORMATION ABOUT THE PERSON NAMED ABOVE, WHOM WE REFER TO BELOW AS "SHE" OR "HER." IF YOU DO NOT KNOW THE INFORMATION, SIMPLY LEAVE THAT SPACE BLANK.

14-15 **1. At what age did <u>she</u> begin menstruating?**

__ __ _____ years

16__ **2. Did <u>she</u> have children?**

1 ☐ No 2 ☐ Yes

↓

17-18 **How old was <u>she</u> when her first child was born?**

__ __ _____ years

19__ **3. Did <u>she</u> have any breast biopsies before her prophylactic mastectomy?**

1 ☐ No 2 ☐ Yes

↓

20-21 **How many breast biopsies did <u>she</u> have before her prophylactic mastectomy?**

__ __ _____ Number of breast biopsies

22__ **Did any of the biopsy results show worrisome findings?**

1 ☐ No 2 ☐ Yes

23__ **4. Did <u>her</u> (blood-related) mother have breast cancer?**

1 ☐ No 2 ☐ Yes 3 ☐ Don't know

↓

24-27 **If yes, in what year?** _____

28-31 **What is <u>her</u> year of birth?** _____

32__ **5. Did <u>she</u> have any blood-related sisters?**

1 ☐ No 2 ☐ Yes

33-34 __ **If yes, how many?** _____

35__ **Have any of <u>her</u> sisters had breast cancer?**

1 ☐ No 2 ☐ Yes

SISTER #1

36-39 **If yes, in what year?** _____

40-43 **What is her year of birth?** _____

SISTER #2

44-47 **In what year?** _____

48-51 **What is her year of birth?** _____

SISTER #3

52-55 **In what year?** _____

56-59 **What is her year of birth?** _____

SISTER #4

60-63 **In what year?** _____

64-67 **What is her year of birth?** _____

SISTER #5

68-71 **In what year?** _____

72-75 **What is her year of birth?** _____

76__ **6. Did <u>she</u> have any blood-related daughters?**

1 ☐ No 2 ☐ Yes

77-78 **If yes, how many?** _____

79__ **Have any of <u>her</u> daughters had breast cancer?**

1 ☐ No 2 ☐ Yes

DAUGHTER #1

80-83 **If yes, in what year?** _____

84-87 **What is her year of birth?** _____

DAUGHTER #2

88-91 **In what year?** _____

92-95 **What is her year of birth?** _____

DAUGHTER #3

96-99 **In what year?** _____

100-103 **What is her year of birth?** _____

DAUGHTER #4

104-107 **In what year?** _____

108-111 **What is her year of birth?** _____

DAUGHTER #5

112-115 **In what year?** _____

116-119 **What is her year of birth?** _____

120__ **7. Have other blood relatives of <u>hers</u>, including men in the family, had breast cancer?**

1 ☐ No 2 ☐ Yes

121__ **If yes, please list relative.**_____

_____

_____

_____

122__ **8. Have any of <u>her</u> blood relatives had ovarian cancer?**

1 ☐ No 2 ☐ Yes

CANCER PROBLEMS

123__ **9. Was <u>she</u> ever diagnosed with breast cancer?**

1 ☐ No 2 ☐ Yes

124-127 **If yes, in what year?** _____ year

128__ **In which breast?** 1 ☐ Right 2 ☐ Left

129-130 **What treatment did she have?** _____

_____

_____

131__ **Did <u>her</u> breast cancer ever spread?**

1 ☐ No 2 ☐ Yes

132-133 **If yes, where?**

_____

134-137 **In what year was this discovered?**

_____ year

138-139 **What treatment did she have?**

_____

_____

_____

10. Did <u>she</u> have any other cancers?

	<u>No</u>	<u>Yes</u>	<u>What year was cancer found?</u>
140-144 **Ovarian cancer**	1 ☐	2 ☐	_____
145-149 **Colon cancer**	1 ☐	2 ☐	_____
150-154 **Uterine cancer**	1 ☐	2 ☐	_____

Other cancer(s) (please list)

155-160 _____	_____
161-166 _____	_____
167-172 _____	_____
173-178 _____	_____

OUTCOMES

179___ **11. After her prophylactic breast surgery, did she have any complications that required additional breast surgery?**

1 ☐ No 2 ☐ Yes

If yes, please indicate the year(s) when she needed repeat surgery and the primary reason below.

	Reason	**Year**
180-185	_____	_____
186-191	_____	_____
192-197	_____	_____
198-203	_____	_____

204___ **12. Did she have any other difficulties with the prophylactic breast surgery that did not require additional surgery?**

1 ☐ No 2 ☐ Yes

If yes, please indicate the year(s) and the difficulty(ies) she experienced.

	Difficulty	**Year**
205-210	_____	_____
211-216	_____	_____
217-222	_____	_____
223-228	_____	_____

229___ **13. What is your relationship to this person?**

1 ☐ Husband
2 ☐ Child
3 ☐ Brother
4 ☐ Sister
5 ☐ Another relative
6 ☐ Friend

Mayo Clinic

200 First Street Southwest Rochester, Minnesota 55905 Telephone 507 284-2511

You had a prophylactic mastectomy (preventive removal of the breast) performed by Mayo Clinic's plastic surgeons. Dr. John E. Woods and Dr. P. G. Arnold from the Department of Surgery at Mayo and I would like to ask you for some information.

We understand that you had a prophylactic mastectomy performed at or near the time that you had your other breast removed because of cancer. Our primary purpose in contacting you at this time is to assess your particular reasons for having had a prophylactic mastectomy and to ask how your health has been following that surgery. In this packet, you will find a form containing questions about your family history of breast cancer, as well as your menstrual and reproductive history. We will also ask about any breast problems that you may have had since your prophylactic mastectomy, including the possibility of any breast cancer on that side or the need for any additional breast surgery. We will also ask you whether you have developed any other cancers.

This follow-up work that we are now doing is part of an approved Mayo Clinic study. We hope that the follow-up information learned through this study will help physicians counsel women in the future as they think about having a prophylactic mastectomy performed. As with your other Mayo Clinic records, the information that you provide us will be kept strictly confidential.

We would like to emphasize that the reason for asking these questions is not that we are concerned about silicone implants causing cancer. Most women who had prophylactic mastectomy at Mayo did so because of a concern about breast cancer. These concerns were based on a variety of reasons, including having had breast cancer in one breast, pre-cancerous change in the breast, a history of breast cancer in the family, or having had multiple prior biopsies for suspicious lumps in the past. These factors are known to increase a woman's risk of a breast cancer to some extent. Some of these factors have also been associated with the development of other types of cancer, such as ovarian cancer or colon cancer. Thus, it is important that we learn of any additional breast cancer problem or other cancer problem that you may have had.

We would like to address the concerns that have been raised in the press about silicone implants and their possible health hazards, including links with breast cancer and several arthritis-like conditions (also called connective tissue diseases). We would like to update you regarding the status of well-controlled medical studies of patients

who have had silicone implants. A recently completed Mayo Clinic study looked at the development of arthritis-like illnesses in Rochester-area women who had silicone-containing implants. Mayo investigators saw no evidence for a link between these implants and any connective tissue disease. These results have been published recently in The New England Journal of Medicine. Moreover, a Canadian group recently studied women who had breast augmentation (or enlargement), with implant placement, for any evidence of increased breast cancer risk later. In fact, these investigators saw fewer breast cancers in women who had implants placed compared with women in the general population (N Engl J Med, Berkel et al, June 18, 1992). This by no means indicates that implants lower risk, but we have no reason to think that they contribute to breast cancer.

We appreciate your help in this study and hope that you are willing to provide the information. If you do not wish to complete the questionnaire, please indicate this below and return this letter since it will make a follow-up call unnecessary. Please understand that current or future medical care at the Mayo Clinic for you and your family members will not be affected by your decision. Specifically, your care will not be jeopardized if you choose not to complete the questionnaire.

If you have family members with breast cancer, and indicate so on the enclosed form, we will be contacting you again for more detailed family information.

We thank you for your consideration.

Sincerely yours,

Lynn C. Hartmann, M.D.
Mayo Women's Cancer Program

John E. Woods, M.D.
Department of Surgery

Phillip G. Arnold, M.D.
Department of Surgery

☐ I do not wish to participate further in this survey.

KPOO

PROPHYLACTIC MASTECTOMY FOLLOW-UP STUDY

SURVEY RESEARCH CENTER

mayo

1-7

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Instructions: Please check the appropriate box or fill in the blank as indicated.

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Month Day Year

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__ __ _____ years

16__ **2. Have you had children?**

1 ☐ No 2 ☐ Yes

17-18 **How old were you when your first child was born?**
_____ years

19__ **3. Did you have any biopsies of the noncancerous breast before your prophylactic mastectomy?**

1 ☐ No 2 ☐ Yes

20-21 **How many biopsies of the noncancerous breast did you have before your prophylactic mastectomy?**

__ __ _____ Number of breast biopsies

22__ **Did any of the biopsy results show worrisome findings?**

1 ☐ No 2 ☐ Yes

23__ **4. Has your (blood-related) mother had breast cancer?**

1 ☐ No 2 ☐ Yes 3 ☐ Don't know

24-27 **If yes, in what year?** _____

28-31 **What is her year of birth?** _____

32___ **5. Do you have any blood-related sisters?**

1 ☐ No 2 ☐ Yes

33-34 ___ **If yes, how many?** _____

35___ **Have any of your sisters had breast cancer?**

1 ☐ No 2 ☐ Yes

SISTER #1

36-39 **If yes, in what year?** _____

40-43 **What is her year of birth?** _____

SISTER #2

44-47 **In what year?** _____

48-51 **What is her year of birth?** _____

SISTER #3

52-55 **In what year?** _____

56-59 **What is her year of birth?** _____

SISTER #4

60-63 **In what year?** _____

64-67 **What is her year of birth?** _____

SISTER #5

68-71 **In what year?** _____

72-75 **What is her year of birth?** _____

76__ **6. Do you have any blood-related daughters?**

1 ☐ No 2 ☐ Yes

77-78 **If yes, how many?** _____

79__ **Have any of your daughters had breast cancer?**

1 ☐ No 2 ☐ Yes

DAUGHTER #1

80-83 **If yes, in what year?** _____

84-87 **What is her year of birth?** _____

DAUGHTER #2

88-91 **In what year?** _____

92-95 **What is her year of birth?** _____

DAUGHTER #3

96-99 **In what year?** _____

100-103 **What is her year of birth?** _____

DAUGHTER #4

104-107 **In what year?** _____

108-111 **What is her year of birth?** _____

DAUGHTER #5

112-115 **In what year?** _____

116-119 **What is her year of birth?** _____

120__ **7. Have other blood relatives of yours, including men in the family, had breast cancer?**

1 ☐ No 2 ☐ Yes

121__ **If yes, please list.**_____

_____

_____

_____

122__ **8. Have any of your blood relatives had ovarian cancer?**

1 ☐ No 2 ☐ Yes

123__ **9. You had cancer in one breast and had the other breast removed for prophylactic (preventive) purposes.**
On the prophylactic side, were you ever diagnosed with breast cancer?

1 ☐ No 2 ☐ Yes

124-127 **If yes, in what year?** _____ year

128-129 **What treatment did you have?** _____

_____

_____

130__ **Did you ever have a recurrence of your breast cancer?**

1 ☐ No 2 ☐ Yes

131-132 **If yes, where?**

_____

133-136 **In what year was this discovered?**

_____ year

137-138 **What treatment did you have?**

_____

_____

_____

10. Have you had any other cancers?

	No	Yes	What year was cancer found?
139-143 **Ovarian cancer**	1 ☐	2 ☐	_____
144-148 **Colon cancer**	1 ☐	2 ☐	_____
149-153 **Uterine cancer**	1 ☐	2 ☐	_____

Other cancer(s) (please list)

154-159 _____ _____

160-165 _____ _____

166-171 _____ _____

172-177 _____ _____

OUTCOMES

11. Please indicate your reason(s) for having prophylactic mastectomy. (Check all that apply.)

178__ A ☐ Cancer in the other breast

179__ B ☐ Family history of breast cancer

180__ C ☐ Lumpy breasts

181__ D ☐ Psychological or emotional, please specify_____

182__ E ☐ Worrisome findings on biopsy

183__ F ☐ Doctor's advice

184__ G ☐ Other reasons not mentioned, please specify_____

_____

12. From those checked above, what do you consider the three most important reasons for having prophylactic mastectomy? (Write the three letters in the spaces below. If you checked only one or two above, order them below and leave the remaining lines blank.)

185__ _____ First most important

186__ _____ Second most important

187__ _____ Third most important

188__ **13. Before your prophylactic mastectomy, what did you think your lifetime risk was of future breast cancer in the noncancerous breast?**

1 ☐ No risk 2 ☐ Low risk 3 ☐ Average risk 4 ☐ High risk 5 ☐ Extremely high risk

189-191 **If you were given a specific figure, please specify.** _____

192__ **14. <u>After</u> your prophylactic mastectomy, what did you think your risk was of a new breast cancer?**

1 ☐ No risk 2 ☐ Low risk 3 ☐ Average risk 4 ☐ High risk 5 ☐ Extremely high risk

193-195 **If you were given a specific figure, please specify.** _____

196___ **15. After your prophylactic breast surgery, did you have any complications that required additional breast-related surgery?**

1 ☐ No 2 ☐ Yes

If yes, please indicate the primary reason for repeat surgery and the year you had the surgery.

	REASON	YEAR
197-202	_____	_____
203-208	_____	_____
209-214	_____	_____
215-220	_____	_____

221___ **Did you have any other difficulties with the prophylactic breast surgery that did not require surgery?**

1 ☐ No 2 ☐ Yes

If yes, please indicate difficulty(ies) and year(s) experienced.

	DIFFICULTY	YEAR
222-227	_____	_____
228-233	_____	_____
234-239	_____	_____
240-245	_____	_____

16. Please indicate how your prophylactic breast surgery affected you in terms of your:

		Greatly increased	Increased	No change	Diminished	Greatly diminished
246___	**Self-esteem**	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
247___	**Satisfaction with your body appearance**	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
248___	**Feelings of femininity**	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
249___	**Sexual relationship(s)**	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
250___	**Emotional concern about developing breast cancer**	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
251___	**Level of stress in life**	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
252___	**Overall emotional stability**	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

253___ **17. Overall, how satisfied are you with your prophylactic mastectomy?**

1 ☐ Very satisfied 2 ☐ Satisfied 3 ☐ Neither 4 ☐ Dissatisfied 5 ☐ Very dissatisfied

254___ **Please explain your reasons for your answer to this question.**

_____

_____

_____

_____

_____

255___ **18. Knowing what you do now, would you choose to have prophylactic mastectomy if you had it to do over again?**

1 ☐ Definitely would 2 ☐ Probably would 3 ☐ Unsure 4 ☐ Probably would not 5 ☐ Definitely would not

256___ **Please explain your reasons for your answer to this question.**

_____

_____

_____

_____

_____

257___ **19. Knowing what you do now, would you choose to have breast reconstruction after prophylactic mastectomy if you had it to do again?**

1 ☐ Definitely would 2 ☐ Probably would 3 ☐ Unsure 4 ☐ Probably would not 5 ☐ Definitely would not

258___ **Please explain your reasons for your answer to this question.**

_____

_____

_____

_____

_____

Unilateral:patient deceased
Appendix III

Mayo Clinic

200 First Street Southwest Rochester, Minnesota 55905 Telephone 507 284-2511

Date

REGARDING: Ms. 8~

Our records indicate that you are the next of kin of Ms. 8~, who had a prophylactic mastectomy (preventive removal of the breast) performed by Mayo Clinic's plastic surgeons. We understand that Ms. 9~ is deceased. Dr. John E. Woods and Dr. P. G. Arnold from the Department of Surgery at Mayo and I would like to extend our sympathy to you and would also like to ask you for some information.

We understand that Ms. 9~ had a prophylactic mastectomy performed at or near the time that she had her other breast removed because of cancer. Our primary purpose in contacting you at this time is to clarify Ms. 9~'s reasons for having had a prophylactic mastectomy and to ask a few health-related questions pertaining to her life after her prophylactic mastectomy. In this packet, you will find a form containing questions about her family history of breast cancer, as well as her menstrual and reproductive history. We will also ask about any breast problems that she may have had following her prophylactic mastectomy, including the possibility of any breast cancer on that side or the need for any additional breast surgery. We will also ask you whether she developed any other cancers.

This follow-up work that we are now doing is part of an approved Mayo Clinic study. We hope that the follow-up information learned through this study will help physicians counsel women in the future as they think about having a prophylactic mastectomy performed. As with Ms. 9~'s other Mayo Clinic records, the information that you provide us will be kept strictly confidential.

If Ms. 9~ had family members with breast cancer, and you indicate so on the enclosed form, we may contact you again about the possibility of obtaining more detailed family information.

We appreciate your help in this study and hope that you are willing to provide the information. If you do not wish to complete the questionnaire, please indicate this below and return this letter since it will make a follow-up call unnecessary. Please understand that current or future medical care at the Mayo Clinic for you and your family members will not be affected by your decision. Specifically, your care will not be jeopardized if you choose not to complete the questionnaire.

We thank you for your consideration.

Sincerely yours,

Lynn C. Hartmann

Lynn C. Hartmann, M.D.
Mayo Women's Cancer Program

John E. Woods, M.D.
Department of Surgery

Phillip G. Arnold, M.D.
Department of Surgery

☐ I do not wish to participate further in this survey.

KPOO

PROPHYLACTIC MASTECTOMY FOLLOW-UP STUDY

SURVEY RESEARCH CENTER

mayo

1-7

Please enter above any missing information or change any that is incorrect.

Instructions: Please check the appropriate box or fill in the blank as indicated.

8-13 **Today's Date** _____/_____/_____
Month Day Year

MEDICAL HISTORY

WE ARE INTERESTED IN THE MEDICAL HISTORY AND FAMILY HISTORY OF WOMEN WHO HAVE CHOSEN TO HAVE A PROPHYLACTIC MASTECTOMY. PLEASE PROVIDE US WITH THE FOLLOWING INFORMATION ABOUT THE PERSON NAMED ABOVE, WHOM WE REFER TO BELOW AS "SHE" OR "HER." IF YOU DO NOT KNOW THE INFORMATION, SIMPLY LEAVE THAT SPACE BLANK.

14-15 **1. At what age did <u>she</u> begin menstruating?**

__ __ _____ years

16__ **2. Did <u>she</u> have children?**

1 ☐ No 2 ☐ Yes

17-18 **How old was <u>she</u> when her first child was born?**
__ __ _____ years

19__ **3. Did <u>she</u> have any biopsies of the noncancerous breast before her prophylactic mastectomy?**

1 ☐ No 2 ☐ Yes

20-21 **How many biopsies of the noncancerous breast did <u>she</u> have before her prophylactic mastectomy?**
__ __ _____ Number of breast biopsies

22__ **Did any of the biopsy results show worrisome findings?**
1 ☐ No 2 ☐ Yes

23__ **4. Did <u>her</u> (blood-related) mother have breast cancer?**

1 ☐ No 2 ☐ Yes 3 ☐ Don't know

24-27 **If yes, in what year?** _____

28-31 **What is <u>her</u> year of birth?** _____

32__ **5. Did <u>she</u> have any blood-related sisters?**

1 ☐ No 2 ☐ Yes

33-34 **If yes, how many?** _____

__ __

35__ **Have any of <u>her</u> sisters had breast cancer?**

1 ☐ No 2 ☐ Yes

SISTER #1

36-39 **If yes, in what year?** _____

40-43 **What is her year of birth?** _____

SISTER #2

44-47 **In what year?** _____

48-51 **What is her year of birth?** _____

SISTER #3

52-55 **In what year?** _____

56-59 **What is her year of birth?** _____

SISTER #4

60-63 **In what year?** _____

64-67 **What is her year of birth?** _____

SISTER #5

68-71 **In what year?** _____

72-75 **What is her year of birth?** _____

76__ **6. Did <u>she</u> have any blood-related daughters?**

1 ☐ No 2 ☐ Yes

77-78 **If yes, how many?** _____

79__ **Have any of <u>her</u> daughters had breast cancer?**

1 ☐ No 2 ☐ Yes

DAUGHTER #1

80-83 **If yes, in what year?** _____

84-87 **What is her year of birth?** _____

DAUGHTER #2

88-91 **In what year?** _____

92-95 **What is her year of birth?** _____

DAUGHTER #3

96-99 **In what year?** _____

100-103 **What is her year of birth?** _____

DAUGHTER #4

104-107 **In what year?** _____

108-111 **What is her year of birth?** _____

DAUGHTER #5

112-115 **In what year?** _____

116-119 **What is her year of birth?** _____

120__ **7. Have other blood relatives of <u>hers</u>, including men in the family, had breast cancer?**

1 ☐ No 2 ☐ Yes

121__ **If yes, please list relative.**_____

_____

_____

_____

122__ **8. Have any of <u>her</u> blood relatives had ovarian cancer?**

1 ☐ No 2 ☐ Yes

CANCER PROBLEMS

123__ **9. She had cancer in one breast and had the other breast removed for prophylactic (preventive) purposes. On the prophylactic side, was she ever diagnosed with breast cancer?**

1 ☐ No 2 ☐ Yes

124-127 **If yes, in what year?** _____ year

128-129 **What treatment did she have?** _____

_____

_____

130__ **Did she ever have a recurrence of her breast cancer?**

1 ☐ No 2 ☐ Yes

131-132 **If yes, where?**

_____

133-136 **In what year was this discovered?**

_____ year

137-138 **What treatment did she have?**

_____

_____

_____

10. Did she have any other cancers?

	No	Yes	What year was cancer found?
139-143 **Ovarian cancer**	1 ☐	2 ☐	_____
144-148 **Colon cancer**	1 ☐	2 ☐	_____
149-153 **Uterine cancer**	1 ☐	2 ☐	_____

Other cancer(s) (please list)

154-159 _____	_____
160-165 _____	_____
166-171 _____	_____
172-177 _____	_____

OUTCOMES

178__ **11. After her prophylactic breast surgery, did she have any complications that required additional breast surgery?**

1 ☐ No 2 ☐ Yes

If yes, please indicate the year(s) when she needed repeat surgery and the primary reason below.

	Reason	Year
179-184	_____	_____
185-190	_____	_____
191-196	_____	_____
197-202	_____	_____

203__ **12. Did she have any other difficulties with the prophylactic breast surgery that did not require surgery?**

1 ☐ No 2 ☐ Yes

If yes, please indicate the year(s) and the difficulty(ies) she experienced.

	Difficulty	Year
204-209	_____	_____
210-215	_____	_____
216-221	_____	_____
222-227	_____	_____

228__ **13. What is your relationship to this person?**

1 ☐ Husband
2 ☐ Child
3 ☐ Brother
4 ☐ Sister
5 ☐ Another relative
6 ☐ Friend